FIGURE 1A

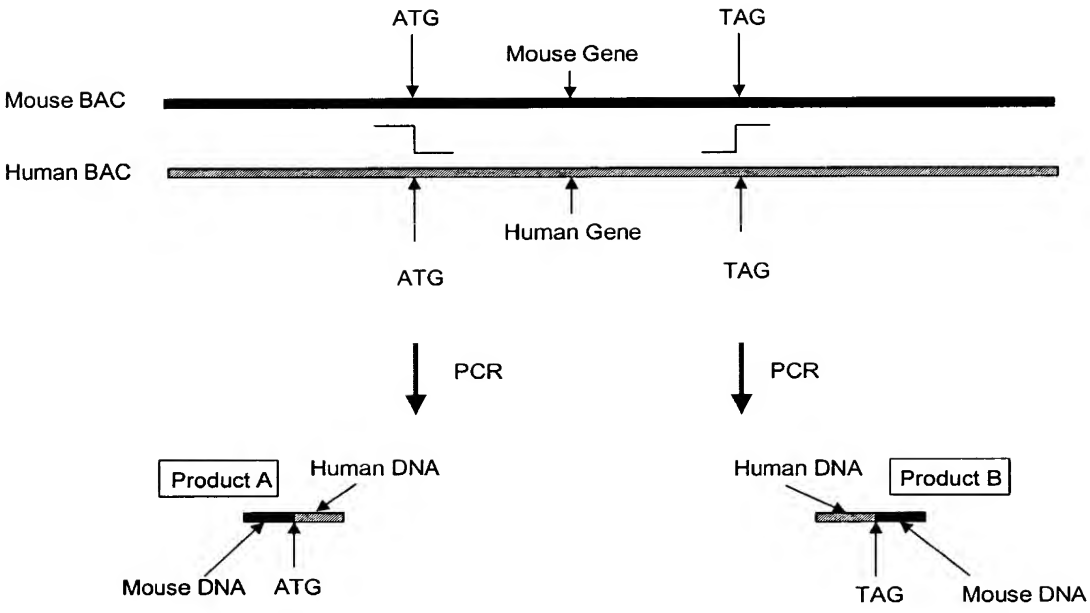

ATG
TAG
Mouse Gene
Mouse BAC
Human BAC
Human Gene
ATG
TAG
PCR
PCR
Product A
Human DNA
Mouse DNA
ATG
Human DNA
Product B
TAG
Mouse DNA

FIGURE 1B

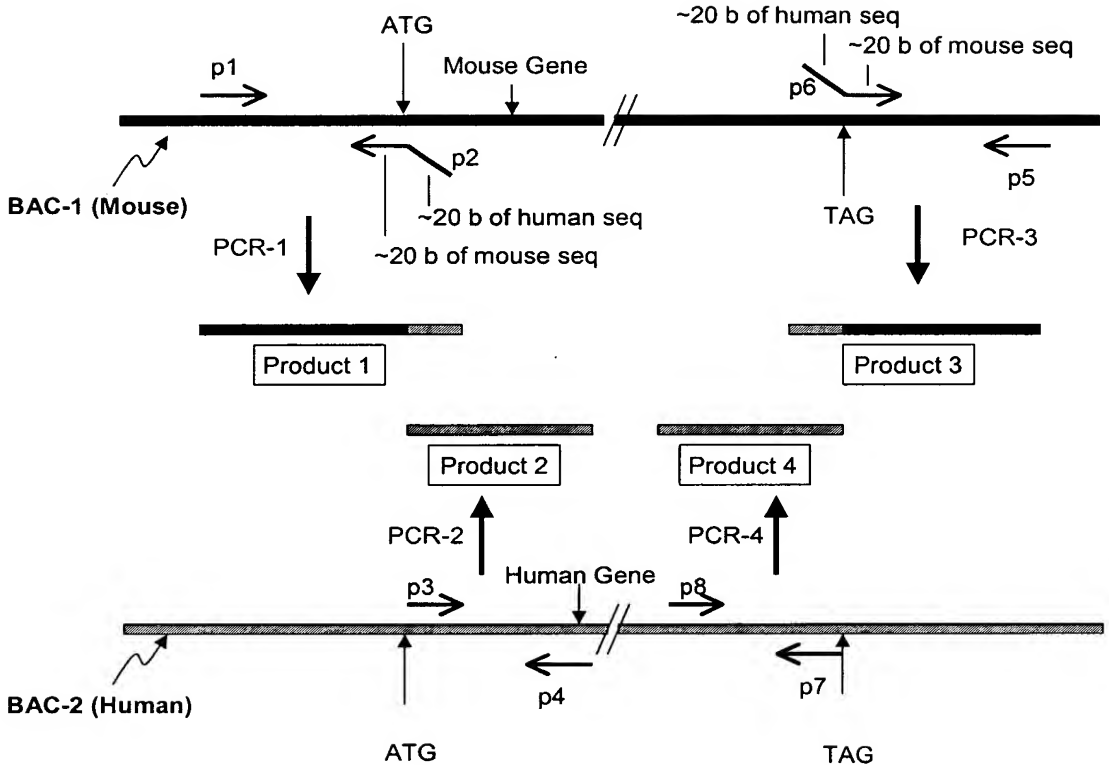

ATG
~20 b of human seq
~20 b of mouse seq
p1
Mouse Gene
p6
p2
p5
BAC-1 (Mouse)
~20 b of human seq
TAG
PCR-1
~20 b of mouse seq
PCR-3
Product 1
Product 3
Product 2
Product 4
PCR-2
PCR-4
Human Gene
p3
p8
p4
p7
BAC-2 (Human)
ATG
TAG

FIGURE 1C

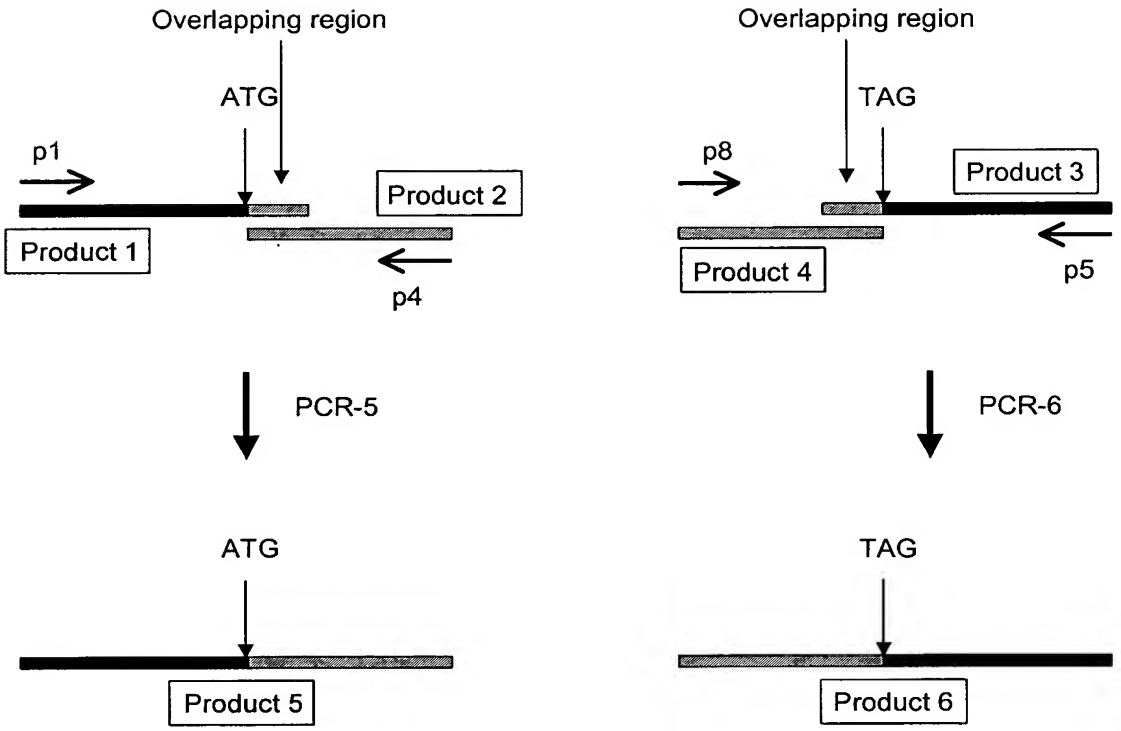

Overlapping region
ATG
p1
Product 2
Product 1
p4
PCR-5
ATG
Product 5
Overlapping region
TAG
p8
Product 3
Product 4
p5
PCR-6
TAG
Product 6

FIGURE 2

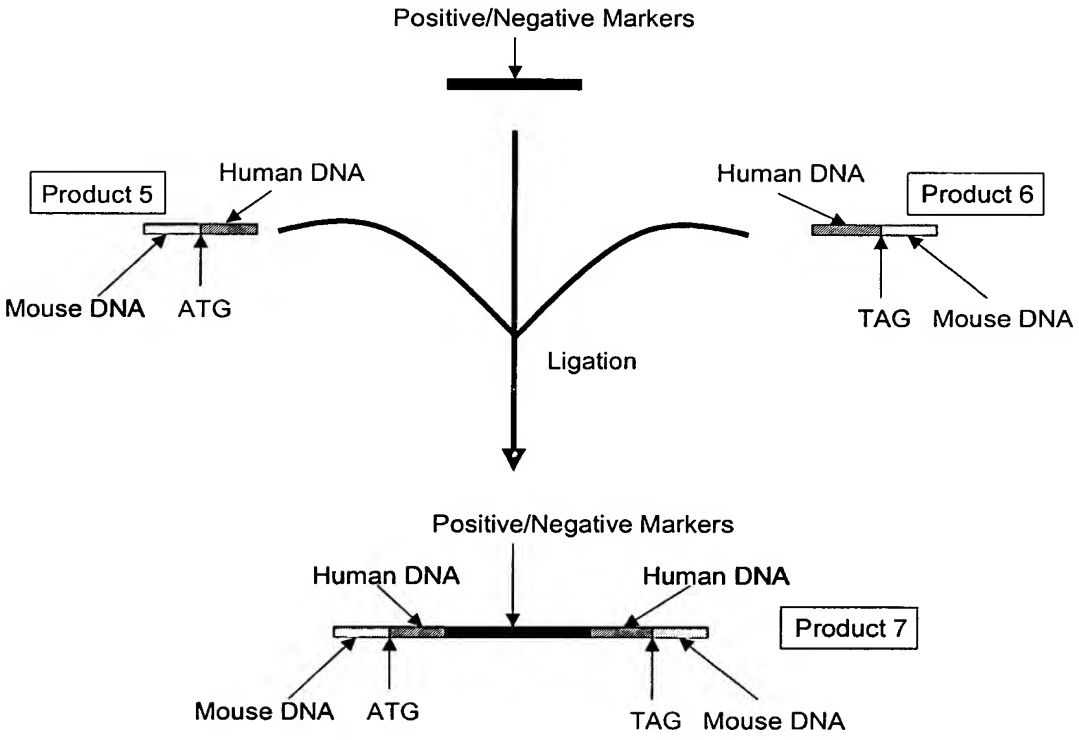

Positive/Negative Markers
Product 5
Human DNA
Mouse DNA
ATG
Human DNA
Product 6
TAG
Mouse DNA
Ligation
Positive/Negative Markers
Human DNA
Human DNA
Product 7
Mouse DNA
ATG
TAG
Mouse DNA

FIGURE 3

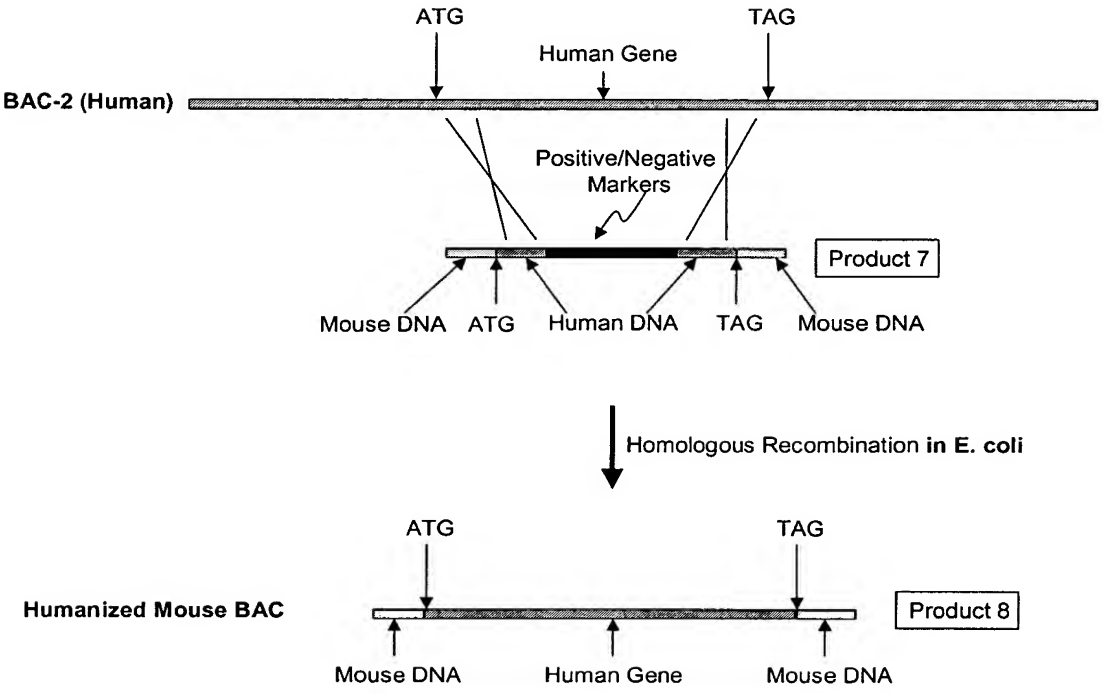

ATG
TAG
Human Gene
BAC-2 (Human)
Positive/Negative Markers
Product 7
Mouse DNA
ATG
Human DNA
TAG
Mouse DNA
Homologous Recombination in E. coli
ATG
TAG
Humanized Mouse BAC
Product 8
Mouse DNA
Human Gene
Mouse DNA

FIGURE 4

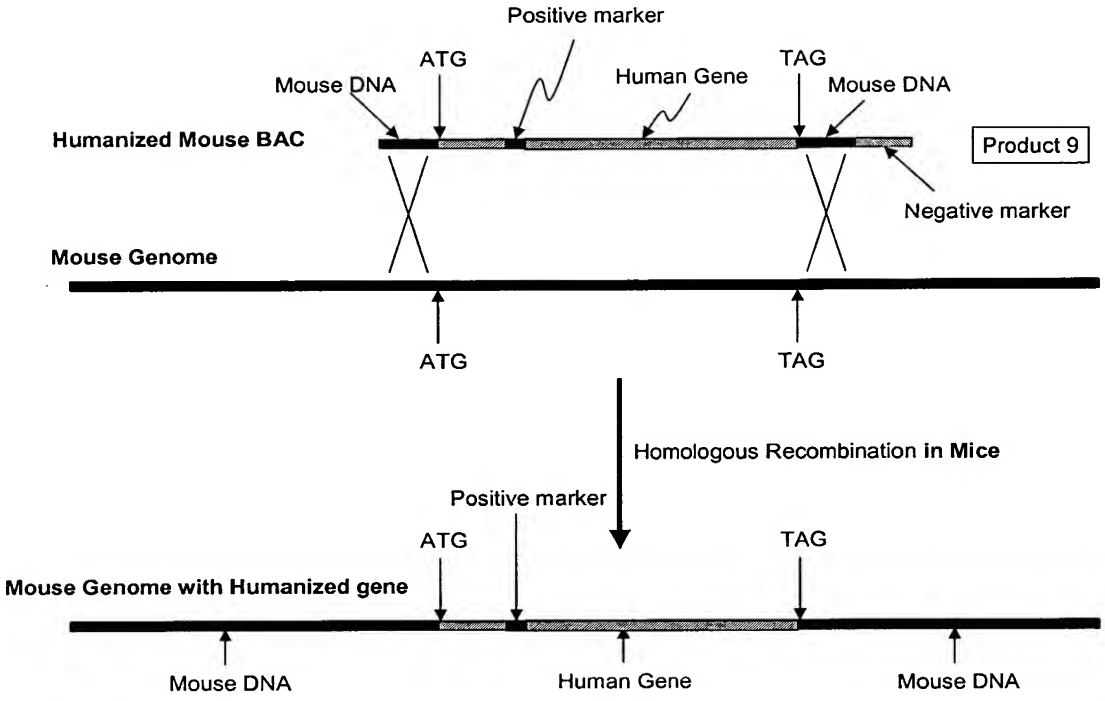

Positive marker
ATG
Mouse DNA
Human Gene
TAG
Mouse DNA
Humanized Mouse BAC
Product 9
Negative marker
Mouse Genome
ATG
TAG
Homologous Recombination in Mice
Positive marker
ATG
TAG
Mouse Genome with Humanized gene
Mouse DNA
Human Gene
Mouse DNA

FIGURE 5A

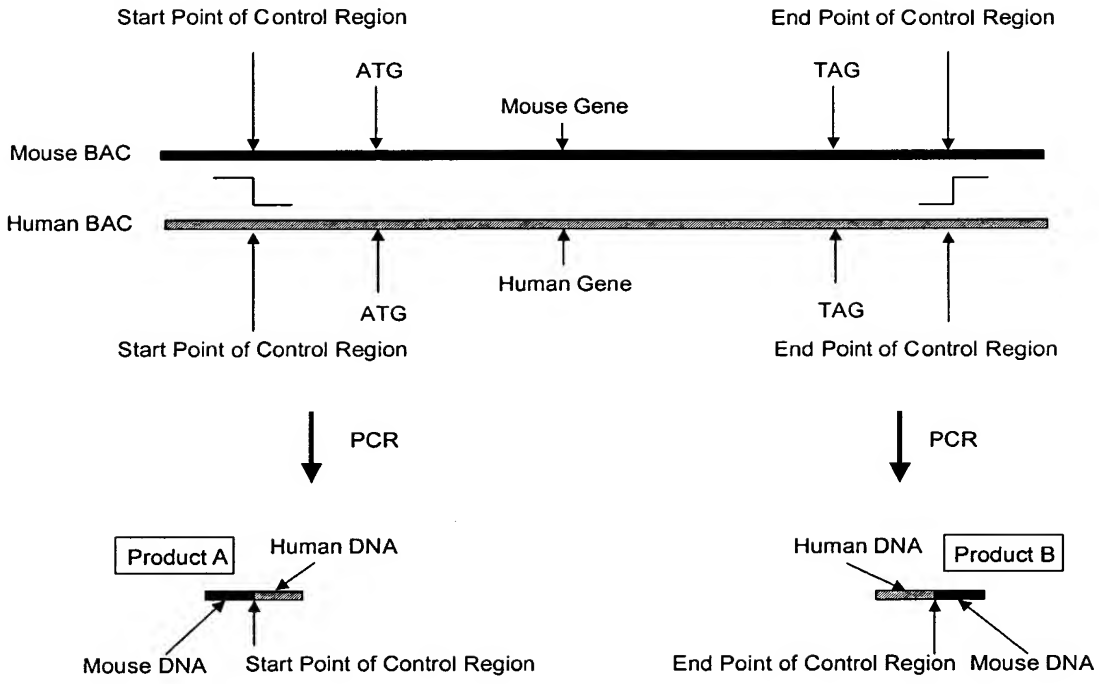

Start Point of Control Region
End Point of Control Region
ATG
TAG
Mouse Gene
Mouse BAC
Human BAC
Human Gene
ATG
TAG
Start Point of Control Region
End Point of Control Region
PCR
PCR
Product A
Human DNA
Human DNA
Product B
Mouse DNA
Start Point of Control Region
End Point of Control Region
Mouse DNA

FIGURE 5B

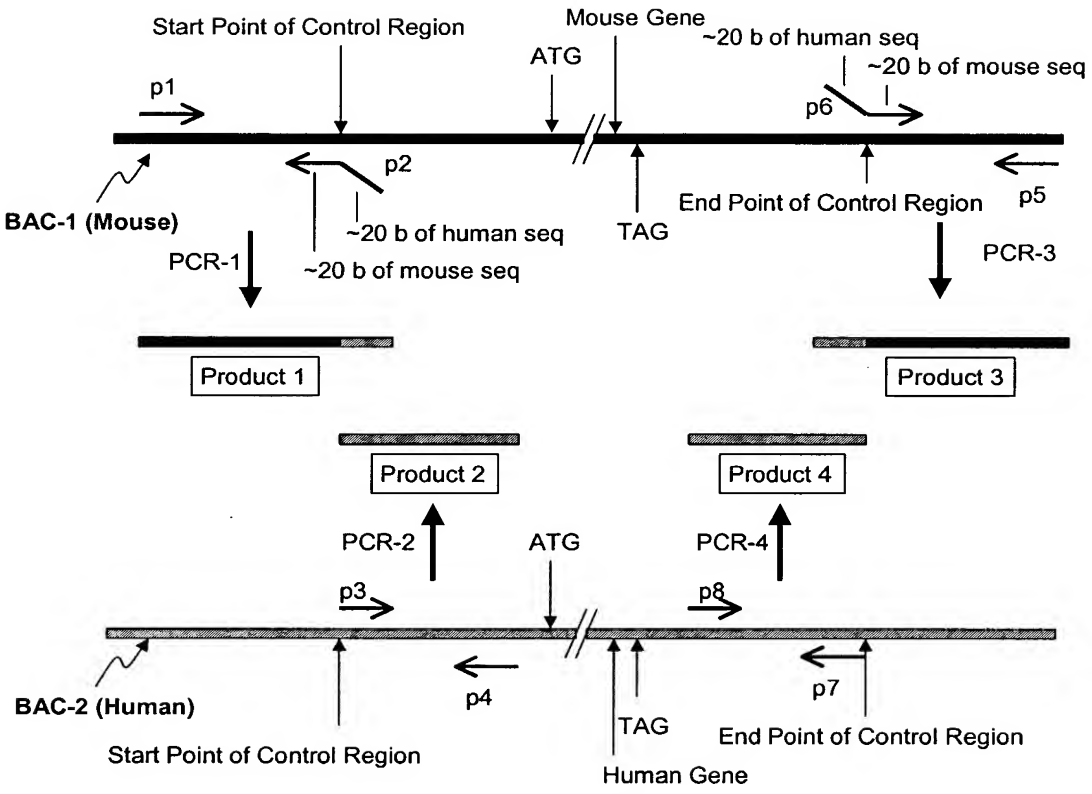

Start Point of Control Region
Mouse Gene
ATG
~20 b of human seq
~20 b of mouse seq
p1
p6
p2
BAC-1 (Mouse)
~20 b of human seq
TAG
End Point of Control Region
p5
PCR-1
~20 b of mouse seq
PCR-3
Product 1
Product 3
Product 2
Product 4
PCR-2
ATG
PCR-4
p3
p8
p4
p7
BAC-2 (Human)
TAG
End Point of Control Region
Start Point of Control Region
Human Gene

FIGURE 5C

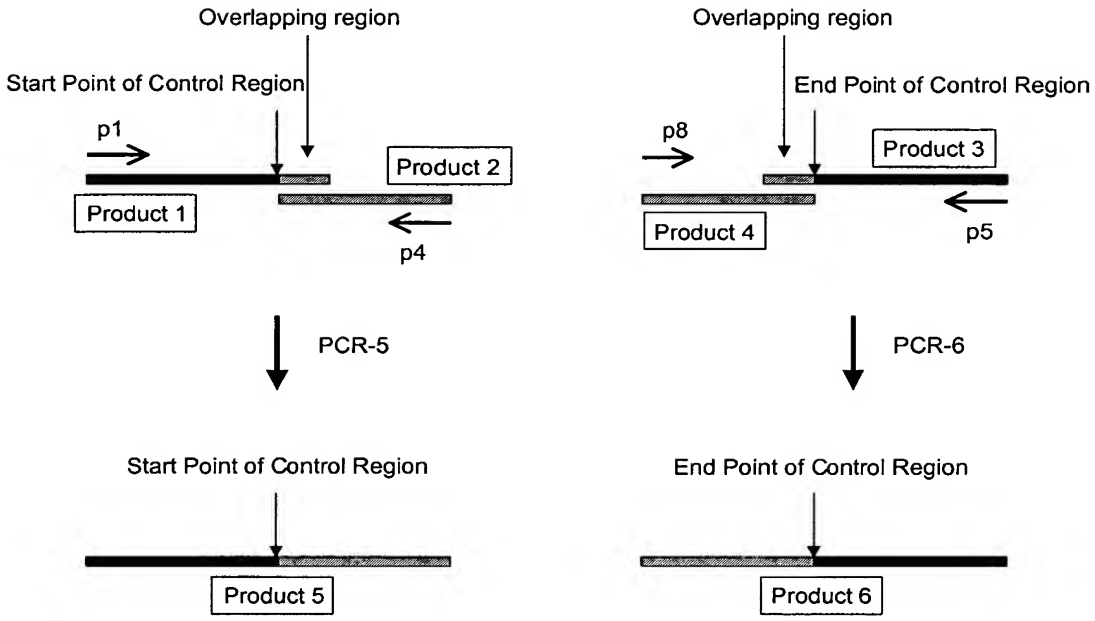

Overlapping region
Start Point of Control Region
p1
Product 2
Product 1
p4
PCR-5
Start Point of Control Region
Product 5
Overlapping region
End Point of Control Region
p8
Product 3
Product 4
p5
PCR-6
End Point of Control Region
Product 6

FIGURE 6

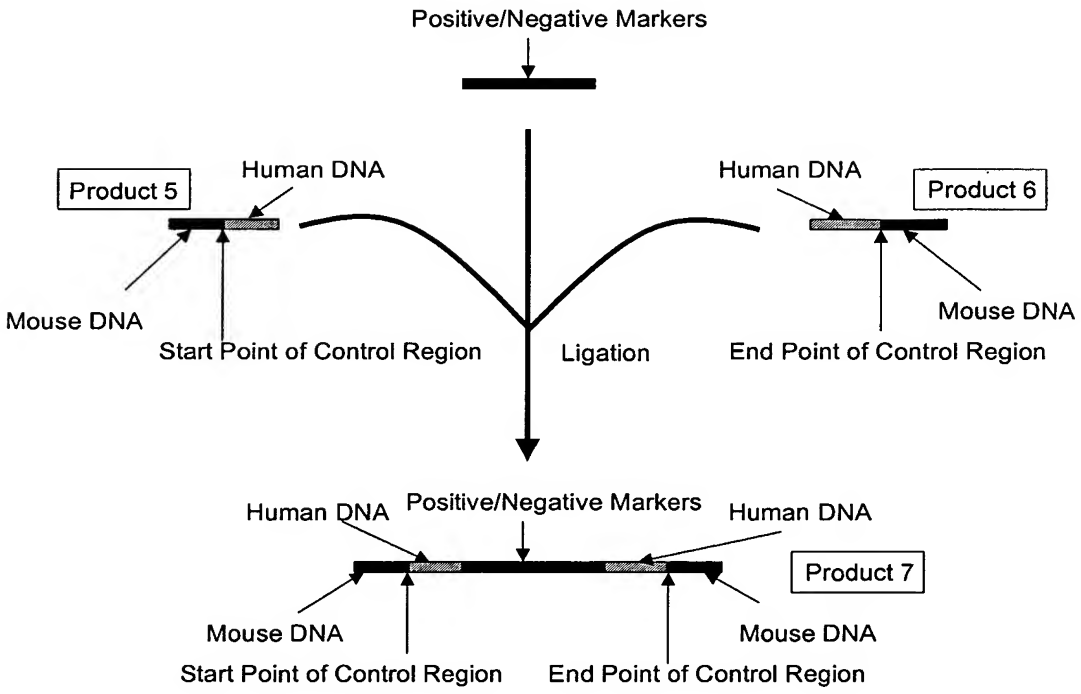

Positive/Negative Markers
Product 5
Human DNA
Human DNA
Product 6
Mouse DNA
Mouse DNA
Start Point of Control Region
Ligation
End Point of Control Region
Human DNA
Positive/Negative Markers
Human DNA
Product 7
Mouse DNA
Mouse DNA
Start Point of Control Region
End Point of Control Region

FIGURE 7

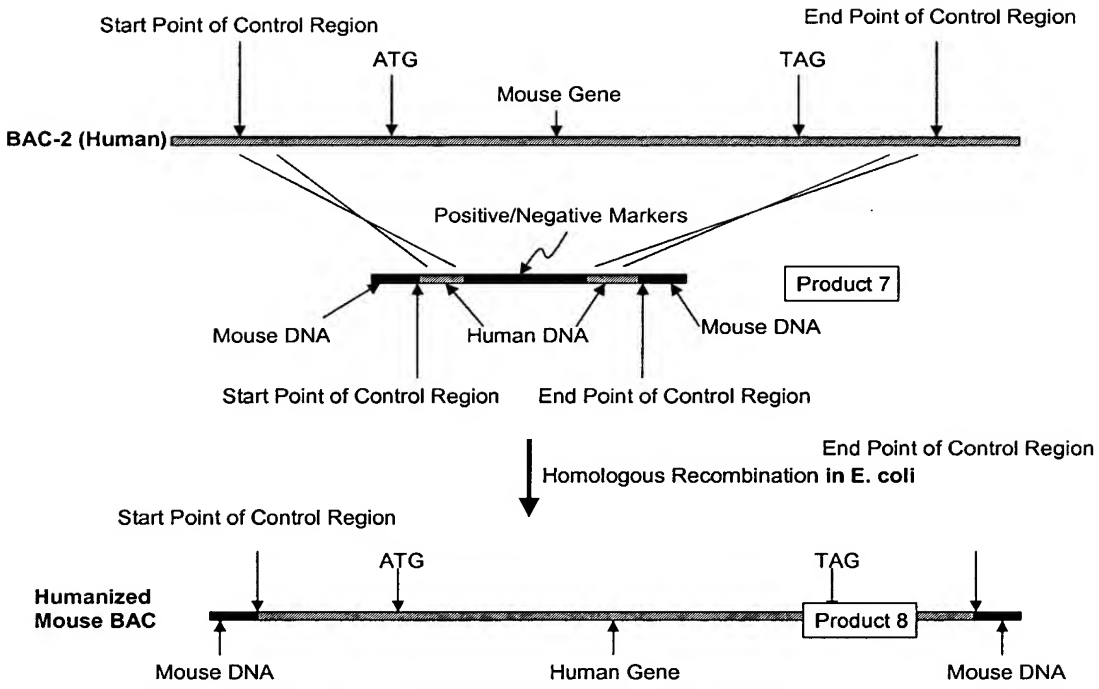
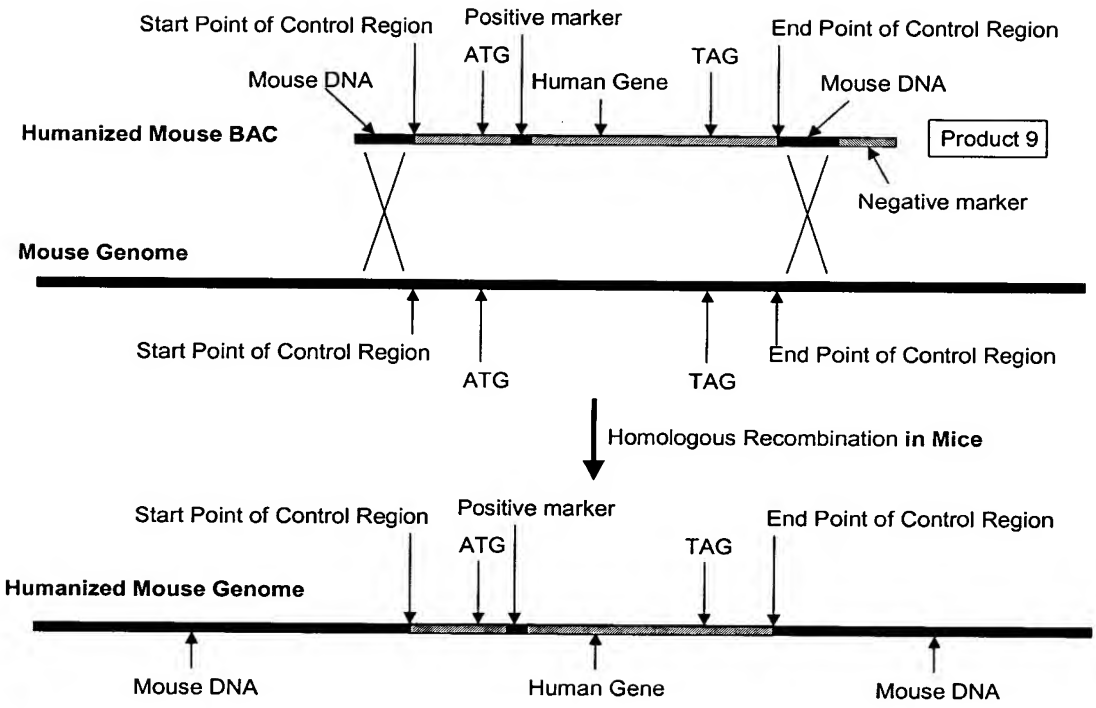

Start Point of Control Region
End Point of Control Region
ATG
TAG
Mouse Gene
BAC-2 (Human)
Positive/Negative Markers
Product 7
Mouse DNA
Human DNA
Mouse DNA
Start Point of Control Region
End Point of Control Region
End Point of Control Region
Homologous Recombination in E. coli
Start Point of Control Region
ATG
TAG
Humanized Mouse BAC
Product 8
Mouse DNA
Human Gene
Mouse DNA

FIGURE 8


Start Point of Control Region
Positive marker
ATG
Human Gene
TAG
End Point of Control Region
Mouse DNA
Mouse DNA
Humanized Mouse BAC
Product 9
Negative marker
Mouse Genome
Start Point of Control Region
ATG
TAG
End Point of Control Region
Homologous Recombination in Mice
Start Point of Control Region
Positive marker
ATG
TAG
End Point of Control Region
Humanized Mouse Genome
Mouse DNA
Human Gene
Mouse DNA

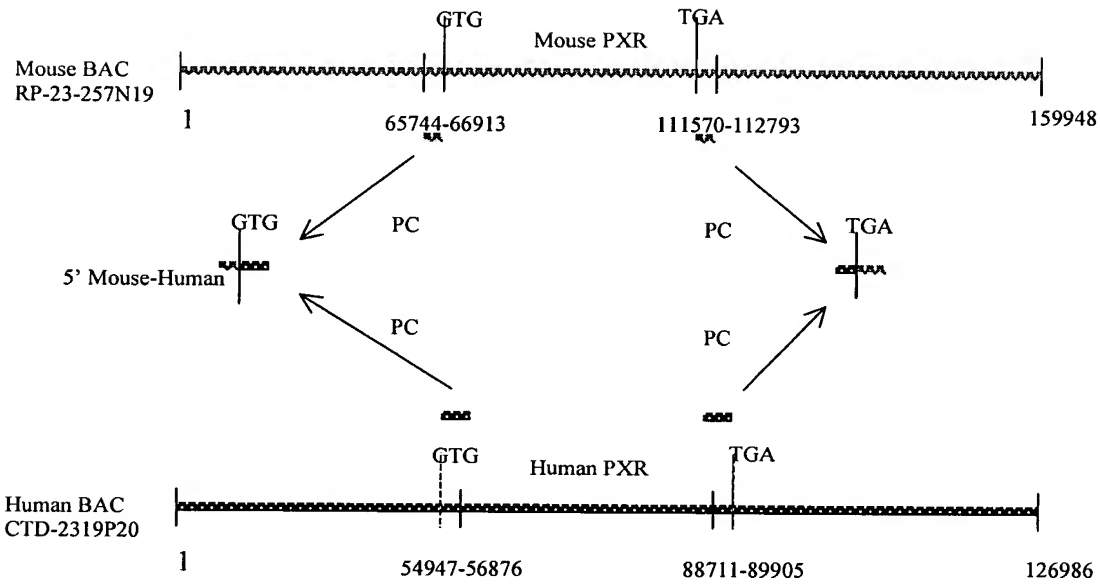

GTG
TGA
Mouse PXR
Mouse BAC
RP-23-257N19
1
65744-66913
111570-112793
159948
GTG
PC
PC
TGA
5' Mouse-Human
PC
PC
GTG
Human PXR
TGA
Human BAC
CTD-2319P20
1
54947-56876
88711-89905
126986

Figure 9

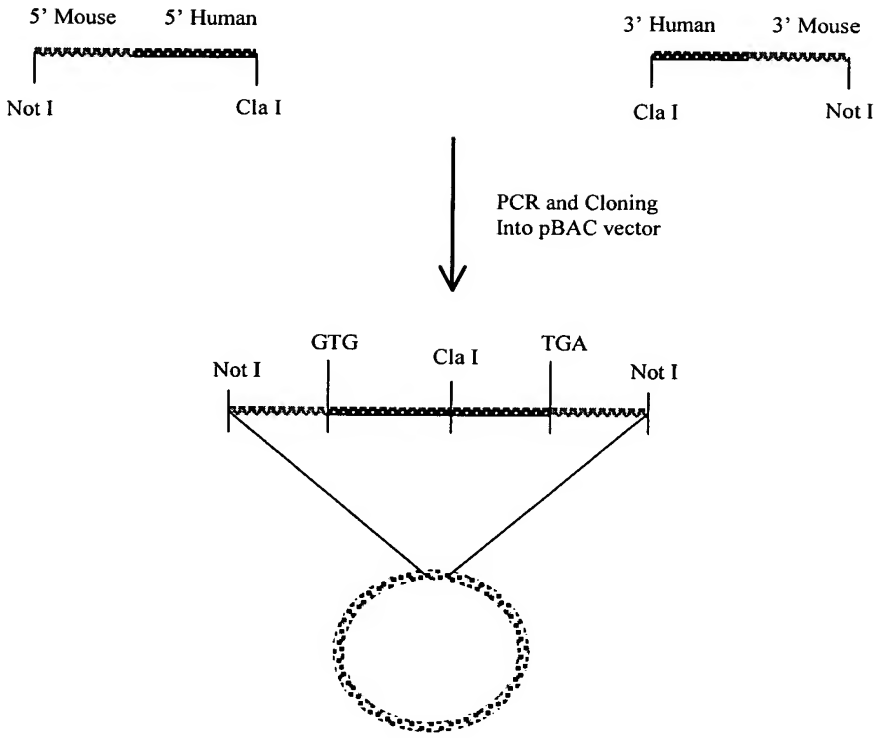

5' Mouse
5' Human
Not I
Cla I
3' Human
3' Mouse
Cla I
Not I
PCR and Cloning
Into pBAC vector
GTG
Cla I
TGA
Not I
Not I

Figure 10

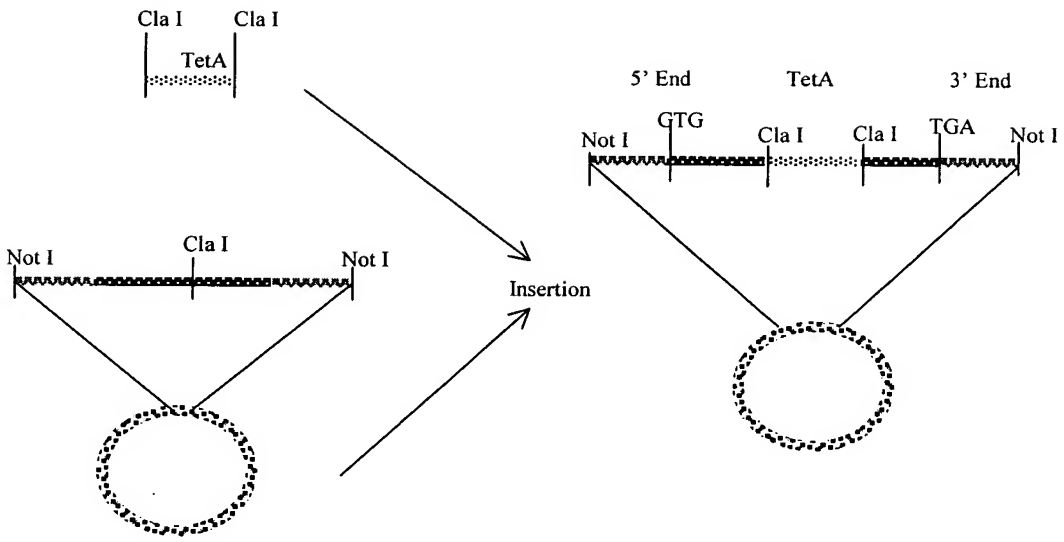

Cla I
Cla I
TetA
Not I
Cla I
Not I
Insertion
5' End
TetA
3' End
GTG
Not I
Cla I
Cla I
TGA
Not I

Figure 11